AT

UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/405,940	09/27/1999	JENNIFER L. HILLMAN	PF-0346-1-DI	1067

27904 7590 04/16/2004

INCYTE CORPORATION
3160 PORTER DRIVE
PALO ALTO, CA 94304

EXAMINER	
EWOLDT, GERALD R	
ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 04/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/405,940	HILLMAN ET AL.	
	Examiner	Art Unit	
	G. R. Ewoldt, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 November 2003 and 09 February 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,13 and 24-27* is/are pending in the application.

4a) Of the above claim(s) *24-26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) *1, 2, 13, 27* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's after final amendment and remarks filed 11/03/03, and the amendment and remarks filed 2/09/04, have been entered.

2. Claims 1, 2, and 13, and newly added Claim 27, are being acted upon.

3. Applicant's request for the rejoinder of "method of use" Claims 24-26 is acknowledged.

4. The specification remains objected to for the introduction of new matter into the specification. In the amendment filed 12/16/02, Applicant removed from the specification the source (specimen number)of the TONGTUT01 cDNA library.

Correction is required in response to this action.

Applicant has indicated that an agreement between Applicant and the Mayo Clinic requires the removal of the specimen number. Applicant requests that the Examiner cite the MPEP rule under which the objection has been made.

Applicant is advised that Applicant's agreements with the Mayo Clinic have no bearing on the examination process. Applicant is advised that MPEP 608.04 states that no new matter may be introduced into a specification. In the instant case, the removal of the specimen number has broadened the disclosure in the "TONGTUT01 cDNA library" might now derive from any source.

5. 35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

6. Claims 1, 2, and 13, and newly added Claim 27 stand/are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility, for the reasons of record set forth in the paper mailed 10/24/00 and maintained in the papers

mailed 4/04/01, 9/09/02, and 7/01/03.

Applicant's arguments, filed 11/03/03 and 2/09/04, have been fully considered but they are not persuasive. Applicant inquires "At the outset, Applicants are confused by the Examiner's reference to Borrebaeck et al., and Page et al. (Office Action of July 1, 2003, page 5). At no point in this case have said references either been presented or discussed by Applicants. Therefore, said references are of no relevance in the present case.

Applicant is advised that the Borrebaeck et al. and Page et al. references are not of record in the instant case and accordingly, are of no instant relevance.

Applicant argues "Applicants again assert the polypeptides of the instant invention are useful at least in two-dimensional polyacrylamide gel electrophoresis ("2-D PAGE") analysis and western blots used to monitor protein expression and assess drug toxicity as would be understood by one of ordinary skill in the art. That these utilities are well-established is well supported by the Furness Declaration, of record."

It remains the Examiner's position that Applicant has not established that 2-D PAGE and western blotting comprise well-established utility in the instant context because the claims are drawn to polypeptides and not 2-D PAGE and western blotting.

Applicant argues "It is an accepted tenent of patent law that a patent application does not disclose, and preferably omits, that which is well known in the art."

Applicant is advised that sufficient disclosure to establish at least utility is required.

Applicant states that drug discovery and expression profiling are not routine tasks, "Instead, their position has always been that those techniques, albeit scientifically complex, were nonetheless well-established, for the reasons already made of record."

It is the Examiner's position that drug discovery and expression profiling are not under examination.

In regard to the Examiner's observation that the facts in the instant case bear little similarity to the fact of *In re Brana*, Applicant argues "While it is true that the invention

claimed in the instant application is of a different class of comoumds [sic] from that claimed in *In re Brana*, both employed homology as evidence of utility."

The Examiner again points out that the case included *in vitro* data which the instant application does not.

Applicants asserts that recent BLAST analysis indicate that the asserted polypeptide of the instant claims is most likely a T cell receptor beta subunit and that said subunit is associated with cancer.

While the asserted polypeptide of the instant claims may be a T cell receptor beta subunit, Applicant has not established its association with any particular cancer, much less the laundry list of cancers disclosed in the specification.

Applicant again argues "The Examiner is correct that Applicants argue that there appear to exist differences in policy verses the law, and that the USPTO'S own Training Materials require a higher standard of utility in the instant application."

Applicant is again advised, as set forth in the previous rejection:

"Applicant is advised that the instant rejection is based on the Examiner's position that the brief sections of the specification devoted to uses of the claimed polypeptide (set forth in their entirety above) do not disclose either a specific and substantial asserted utility or a well-established utility as is required by the statute."

Applicant has submitted additional 1.132 declarations of Dr. John Rockett and Dr. Vishwanath Iyer. Those declarations are addressed here.

Dr. Rockett describes the value of DNA microarrays, in particular the Declarant indicates the value of such arrays to toxicologists. The Declarant concludes, "expression profiling in toxicology studies yield patterns of changes that are characteristic of an agent of unknown toxicity, which patterns may usefully be matched to those of well-characterized toxins... In the context of such patterns of gene expression, each additional gene-specific probe provides an additional signal that could not otherwise have been detected, giving a more comprehensive, robust, higher resolution -- and thus more useful -- pattern than otherwise would have been possible".

It is noted that the declaration lacks *any* information regarding the asserted TCRLP (sometimes also apparently referred to as TCRLB) polypeptide. It is the Examiner's position that the value of microarrays in toxicology and drug testing is not under examination - the value of the asserted polypeptide of the instant specification in said processes is. It is the Examiner's position that Applicant has failed to establish said value. The Declarant does make the argument that each additional gene probe in a microarray *might* provide more useful results, however, this conclusion alone provides no particular utility for the specific asserted polypeptide of the instant invention.

Dr. Vishwanath Iyer describes additional uses for microarray-based expression profiling. In particular, the Declarant describes the use of microarrays in establishing drug signature patterns. In describing the value of each probe on an array, the Declarant states "our ability to subdivide cancers into discriminable classes by expression profiling is limited by the resolution of the patterns produced. With more genes contributing to the expression patterns, we can potentially draw finer distinctions among the patterns, thus subdividing otherwise indistinguishable cancers into a greater number of classes; the greater the number of classes, the greater the likelihood that the cancers classified together will respond similarly to therapeutic intervention, permitting better individualization of therapy and, we hope, better treatment outcomes...If a gene does not change expression in an experiment, or if a gene is not expressed and produces no signal in an experiment, that is not to say that the probe lacks usefulness on the array; it only means that an insufficient number of conditions have been sampled to identify expression changes. In fact, an experiment showing that a gene is not expressed or that its expression level does not change can be equally informative."

Much like Dr. Rockett, Dr. Iyer extolls the virtues of microarrays. Just like Dr. Rockett, Dr. Iyer adds nothing regarding the asserted TCRLP (or TCRLB) polypeptide of the instant claims. Again, microarrays are not under examination. And again, regarding the argument that more individual probes are better, this conclusion alone provides no particular utility for the specific asserted polypeptide of the instant invention. Just as more bolts and rivets would build a larger airplane, no matter how many individual bolts and rivets there are, the size and complexity of the airplane says little about each individual bolt or rivet.

Applicant again cites *Brenner v. Manson*, 383 U.S. 519,532 (1966), presumably in support of the invention of the instant claims. Yet, as set forth previously, in *Brenner v. Manson*, the court concurred with the position of the Board of Appeals that "It is our view that the statutory requirement of usefulness of a product cannot be presumed merely because it happens to be closely related to another compound which is shown to be useful." While the claims in question recited a process, the court found that neither a product nor a process of making said product, were considered useful simply because "the compound yielded belongs to a class of compounds now under serious scientific investigation." And in the now famous and often quoted conclusion, it was set forth that "But a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion."

Applicant argues "Applicant has submitted facts and evidence in their response filed November 3, 2003 which showed that the utility of the claimed TCRLP polypeptides is not limited to said polypeptides merely serving as a component of an assay for monitoring gene expression. Applicant' facts show, in particular: (1) how persons of ordinary skill in the art would have known to use, and would have known how to use, TCRLP polypeptides as disease markers for cancers, particularly T-cell leukemias and T-cell lymphomas and for other uses, regardless of the polypeptide's biological function; (2) the skilled artisan would have known to use, and how to use data generated by expression analysis using the TCRLP polypeptides for toxicology assessments, in drug development, and for molecular phenotyping (TCRLP likely maps to the T cell receptor beta subunit gene cluster on chromosome 7), not withstanding the polypeptide's biological function; and (3) that the uses for both the TCRLP polypeptides are not limited to expression analysis."

Applicant is advised that, regarding assertion (1), Applicant is simply mistaken, there are no "facts" of record as to how the asserted polypeptides could be specifically used as markers for any cancer. Regarding assertion (2), it is the Examiner's position that there is no evidence of record indicating how the asserted TCRLP (sometimes TCRLB) polypeptide would be used in any specific toxicology test or in any specific drug development methods, regardless of the asserted polypeptide gen's "likely" chromosomal location. Regarding assertion (3), no specific non-"expression analysis" are disclosed. Indeed, no specific uses of any kind are disclosed.

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1, 2, and 13, and newly added Claim 27 stand/are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific or substantial asserted utility or a well-established utility for the reasons set forth above, one skilled in the art would not know how to use the claimed invention so that it would operate as intended without undue experimentation, for the reasons of record set forth in the paper mailed 10/24/00 and maintained in the papers mailed 4/04/01, 9/09/02, and 7/01/03.

Applicant's arguments, filed 11/03/03 and 2/09/04, have been fully considered but they are not persuasive. Applicant argues that "To the extent that the rejection under § 112, first paragraph, is based on the improper allegation of lack of patentable utility under § 101, it fails for the same reasons."

See the Examiner's response in the previous section.

9. Claim 2, and newly added Claim 27 stand/are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor, at the time the application was filed, had possession of the claimed invention, for the reasons of record set forth in the paper mailed 10/24/00 and maintained in the papers mailed 4/04/01, 9/09/02, and 7/01/03.

Applicant requests a clarification as to why Claim 1 no longer appears to be rejected for lack of adequate written description.

Applicant is advised that due to a previous amendment removing "variant" from Claim 1, the claim is no longer rejected for lack of adequate written description.

Applicant's arguments, filed 11/03/03 and 2/09/04, have been fully considered but they are not persuasive. Applicant argues "Applicants reiterate their arguments filed December 9, 2002, including the references to Exhibits A and B, supplemental evidence provided by Applicants to illustrate the presence of the immunoglobulin functional domains found within TCRLP and two other TCR proteins, gi 1100182 and gi 339012. This evidence was apparently neither considered nor acknowledged by the Examiner. Clearly, it appears that the Examiner has confused this instant application and the responses filed by Applicants with those by another. Applicants respectfully request that the Examiner fully review the response filed December 9, 2002, especially pages 29-31 and the afore mentioned exhibits as it pertains to the written description rejection."

Applicant is advised that all evidence presented by Applicant has been given all due consideration. Applicant is advised that it remains the Examiner's position that said evidence has not provided sufficient written description for all of the variants encompassed by the instant claims.

Applicant reiterates the minimal disclosure of the specification and indicates disagreement with the Examiner's position that an adequate written description has not been set forth. Applicant indicates that the disclosure of "at least 90% identical to the amino acid sequence of SEQ ID NO:1" comprises an adequate "structural" description and refers to it as "other appropriate language". Applicant argues that the assay of Example X can be used to identify functional variants. Applicant argues that "Applicants submit that this description is sufficient to describe the claimed genus based on the disclosure of the single species, SEQ ID NO: 1".

Applicant is advised that it remains the Examiner's position that the single species disclosed in the specification does not adequately describe the claimed genus, despite Applicant's argument that "at least 90% identical to the amino acid sequence of SEQ ID NO:1" comprises an adequate "structural" description. Regarding the IL-2 assay of example X, the "example" merely states that an assay of IL-2 activity can be performed to establish IL-2 activity. This "assay", even in combination with Applicant's asserted "structural" disclosure, provides an inadequate written description for the claimed variants.

10. The following are new grounds of rejection.

11. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

12. Claim 27 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, specifically, the phrase "a polypeptide comprising a naturally occurring an amino acid..." is not grammatically correct. The "an" should be deleted.

13. Claim 27 is rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. This is a new matter rejection.

The specification and the claims as originally filed do not provide support for the invention as now claimed, specifically: "an immunogenic fragment of a polypeptide having the amino acid sequence of SEQ ID NO:1".

Applicant indicates that support for the claim can be found in the specification at pages 7 and 8. A review of the specification discloses fragments which are "immunologically active", but not "an immunogenic fragment".

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Dr. Gerald Ewoldt whose telephone number is (571) 272-0843. The examiner can normally be reached Monday through Thursday from 7:30 am to 5:30 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841.

16. **Please Note**: Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications

is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). Inquiries of a general nature may also be directed to the Technology Center 1600 Receptionist at (571) 272-1600.

G.R. Ewoldt, Ph.D.
Primary Examiner
Technology Center 1600

4/15/04
G.R. EWOLDT, PH.D.
PRIMARY EXAMINER